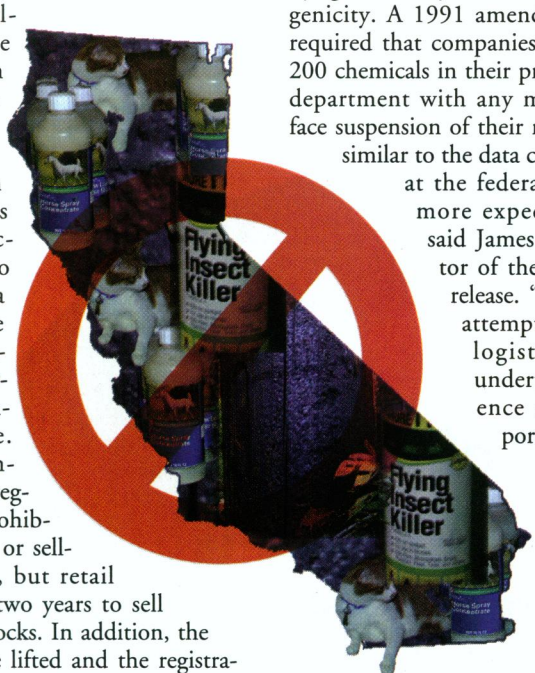
The smart ones are going green, the dumb ones are not, and the foolish ones are pretending.
David Krents, on corporate environmental policy, quoted in *Globe and Mail* (Toronto) 13 October 1990

Forum

California Bans Pesticides

After requesting that studies be submitted on the toxicity of 200 chemicals commonly used in pesticides, officials at the California Department of Pesticide Regulation (DPR) have decided that not enough is known about three of these chemicals to allow their continued use in the state. By the beginning of October, the manufacturers of 23 pesticide products that contain these chemicals will have been notified by the department that their products are no longer registered for manufacture or sale in California, according to Veda Federighi, communications director for the DPR.

The suspension will involve products containing the fungicide chloreneb, the wood preservative creosote, and aromatic petroleum distillates, which are commonly used in insecticides. The DPR said it is suspending products that contain these compounds because manufacturers failed to comply with a March 30 deadline for submitting toxicity studies showing that the compounds are safe. After the suspension takes effect, registrants will be prohibited from making or selling the products, but retail dealers will have two years to sell their remaining stocks. In addition, the suspension will be lifted and the registration reinstated if manufacturers submit all required studies after the suspension takes effect or if the manufacturer can show that use of the chemical results in insignificant human exposure.



According to Jacqueline Fernette, coordinator of corporate communication for Reilly Industries, Inc., one of the companies that sold creosote products in California, her company simply decided that completing the requested toxicity studies was not cost efficient. "[The suspension] certainly effects Reilly, but in a small way," Fernette said. "We tried, along with other suppliers, to get [California] to accept testing we were currently doing for the EPA, but apparently they didn't feel it was sufficient." Fernette said that creosote is not a particularly hazardous chemical, but that "it is a chemical that must be dealt with appropriately."

The process of collecting data on the 200 chemicals came about as a result of the 1985 Birth Defects Prevention Act (SB 950), which mandated that the state collect data on all pesticide active ingredients so that potential chronic health effects could be evaluated. For each pesticide ingredient, 10 studies are usually required, including animal studies on chronic toxicity, oncogenicity, teratogenicity, reproductive toxicity, genotoxicity, neurotoxicity, and mutagenicity. A 1991 amendment to the law required that companies using any of the 200 chemicals in their products supply the department with any missing studies or face suspension of their registrations. "It is similar to the data collection going on at the federal level, but on a more expedited schedule," said James W. Wells, director of the DPR, in a press release. "No state has ever attempted to master the logistics of such an undertaking or the science required to support it."

Though almost all data have been submitted, Federighi says, "The real work of SB 950 begins now." According to Federighi, scientists at the DPR must now review all submitted studies and make sure that the data are adequate according to EPA guidelines. Next, the data will be scanned for any significant adverse effects brought to light by the studies. "Based on our findings," Federighi said, "we will . . . prioritize the chemicals for risk assessment. If we get something that's a real red flag, we will act on it immediately." After it is finished dealing with all 200 "priority chemicals," the department must then face the larger task of going through the same process for all other pesticide active ingredients.

Chloroneb, creosote, and aromatic petroleum distillates are not the only three pesticide ingredients out of the original 200 that will no longer be registered with the DPR for use in California. As a result of the SB 950 legislation, registrations were not renewed or were withdrawn by the manufacturers of products containing 44 other active ingredients. Some of these registrants withdrew their products rather than pay for costly toxicological testing, although, according to the DPR, other factors were often involved. Products containing seven other active ingredients had their registrations revoked for failure to comply with earlier data submission requirements.

All data requirements have been met for 144 compounds, including diphacinone and formaldehyde, which were in danger of suspension earlier this year. Because of 1996 legislation, studies on two chemicals, methyl bromide and pentachlorophenol, are not due until December 1997.

Federal Agencies Scrutinize Lung Surgery

When St. Louis surgeon Joel Cooper began experimenting with a new form of lung surgery in 1993, emphysema patients rejoiced. For many, his lung volume reduction surgery (LVRS) offered their only hope for resuming a normal life. Traditional treatment, with drugs and rehabilitation, provides only temporary relief and, while lung transplant offers a cure, its high risk severely limits its use.

As news of Cooper's promising surgery spread, surgeons nationwide adopted his technique. More than 3,000 emphysema patients had received LVRS by December 1995, when officials from the Health Care Financing Administration made the surprising announcement that Medicare would no longer cover the costly procedure. "There [were] not enough data for us to assess the risks and benefits," explained Steven Sheingold, director of HCFA's technology and special analysis staff.

HCFA's decision prompted a flurry of protest from many of the 2 million Americans suffering from emphysema. Last April, HCFA officials announced they

would resume payment in 1997, but only for a limited number of patients participating in a seven-year study to be conducted by the National Institutes of Health.

HCFA's announcement stirred up strong sentiments among medical professionals accustomed to hashing out the pros and cons of new procedures among themselves. Many agree on the need for further research. Others, however, dismiss the study as a political move to cut costs. Lung reduction surgery costs between $35,000 and $70,000.

Although often considered new, LVRS dates back to the late 1950s, when University of Maryland surgeon Otto Brantigan performed the surgery on 33 patients. Brantigan theorized that emphysema patients would breathe more easily with smaller lungs. An emphysematous lung expands as the disease breaks down the walls in the spongy organ's air sacs. Pressure from the distended lungs prevents the diaphragm from pushing air out effectively. By reducing the lungs' size, Brantigan believed he could improve the mechanics of the breathing muscles. Unfortunately, he had no means of measuring his patients' improvement. His procedure was largely forgotten until its recent revival, led by Cooper at Barnes Hospital in St. Louis.

Cooper typically splits his patients' sternums and uses a scalpel to remove 20–30% of each lung. His first 20 patients demonstrated a remarkable 82% increase in their forced expiratory volume, the amount of air they can blow out. Seventy-one percent were able to give up supplemental oxygen. Other surgeons report substantial improvements in at least two-thirds of their LVRS patients. "Our patients feel dramatically better and breathe better," said John Chen, assistant chief of cardiothoracic surgery at the University of California–Irvine Medical Center.

But what about the minority of patients who fail to improve, and the 5–10% who die? Will patients who have had the surgery live any longer than those receiving traditional treatment with drugs and rehabilitation? These are among the questions NIH officials expect their study to answer. The NIH's National Heart, Lung and Blood Institute will manage the study, which is slated to begin in 1997. Approximately 15 medical centers will be chosen to conduct clinical trials. Approximately 3,000 patients will participate. All will receive intensive pulmonary rehabilitation and drug therapy. Half, chosen at random, then will undergo LVRS. Researchers will compare the progress of the two groups.

Those who support the study point out the need for more data. "We should know up front who improves and who does not," said Jonathon Truwit, interim division chief of pulmonary and critical care medicine at the University of Virginia in Charlottesville. "If we're setting these patients' clocks back, let's find out how far back."

Pulmonologist and ethicist Mark Tonelli of the University of Washington in Seattle pointed out the government's success in regulating the pharmaceutical industry. "If this were a new drug, instead of a new type of surgery, the Food and Drug Administration would require extensive testing," he said. "I think the study is a good model."

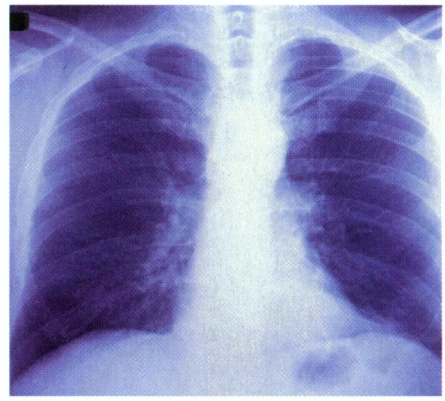
Critics object to the random selection that will deny surgery to half the candidates. They say drugs and rehabilitation have never produced the dramatic improvements seen in some LVRS patients. "We see this as a government ploy to hold back expenses," said Rodney Landreneau, head of thoracic surgery at Allegheny General Hospital in Pittsburgh.

HCFA's Sheingold countered, "We do not base our decisions on cost. We base our decisions on effectiveness. However, we're all forced to assure the highest quality of care while containing costs." Sheingold added that the LVRS study may be just a hint of future government oversight of surgical procedures. "HCFA and the NIH are looking into studying other areas, including kidney/pancreas transplants," he said. "This is a long overdue marriage of the payment agency and the best scientific agency to provide data about what works in health care."

Promising Lung Cancer Vaccine

An antibody developed by researchers at Memorial Sloan-Kettering Cancer Center (MSKCC) appears to prolong the lives of patients with small cell lung cancer. Patients who received injections containing the antibody BEC2 and *Mycobacterium bovis*, a strain of bacteria that stimulates the immune system, were found to live longer than patients who received only the standard treatment for small cell lung cancer, which is chemotherapy with or without radiation. Small cell lung cancer is usually fatal, with a 15–20% long-term survival rate for patients in whom the cancer is contained to the chest, and only a 0–5% long-term survival rate for those in whom the cancer has spread beyond the chest. The current median survival period, for patients diagnosed with small cell lung cancer, is 7–14 months.

To create BEC2, the researchers emulated the structure of GD3 ganglioside, a nonprotein molecule found in certain cancer cells, such as small cell lung and melanoma. GD3 is not recognized by the body as a foreign molecule and therefore does not usually trigger an immune response, says Stefan Grant, an attending physician at MSKCC and co-principal investigator of the project to develop the antibody. The researchers found that BEC2 is recognized as foreign and, because their structures are similar, stimulates the production of antibodies against both BEC2 and GD3. The antibodies signal the immune system to destroy the cells containing GD3 and BEC2, thus eliminating the cancer.



A shot in the lungs. A new antibody may help patients with small cell lung cancer live longer.

MSKCC researchers conducted a clinical trial on eight patients with small cell lung cancer who had received chemotherapy. The researchers administered the vaccine to the participants five times during a period of 10 weeks. Six of the participants completed the immunizations and were evaluated, and four of these were found to be free of the cancer and healthy three years after their diagnoses.

The control group for this study consisted of 34 patients who had received similar chemotherapy at MSKCC. The median survival for this group was 16.2 months, whereas the median survival for the group treated with BEC2 was more than 36 months. The study was presented at the American Society of Clinical Oncology annual meeting in May in Philadelphia.

The only side effect seen thus far is a local reaction at the site of the injections, which is manifested by inflammation and leaves a scar, said Grant. MSKCC researchers are now planning a larger study to test the vaccine. "We are planning a large randomized phase-3 trial, which we anticipate [to be conducted] towards the middle of next year," Grant said. The study will involve more patients and a larger control group.

Although the vaccine has not yet been thoroughly tested, MSKCC researchers are